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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/722,869	11/26/2003	Kevin R. Stone	CROL-156 (56290-103)	8648
7590	09/22/2004		EXAMINER MAYER, SUZANNE MARIE	
Mark G. Lappin McDermott, Will & Emery 28 State Street Boston, MA 02109			ART UNIT	PAPER NUMBER
			1653	

DATE MAILED: 09/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

10/722,869

**Applicant(s)**

STONE, KEVIN R.

**Examiner**

Suzanne M. Mayer, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-23 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-23 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |  |
|---|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. ____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)            |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date ____ | 6) <input type="checkbox"/> Other: ____  |

## DETAILED ACTION

### *Priority*

1. It is noted that this application appears to claim subject matter disclosed in prior Application No. 60/429,078, filed 11/26/2002. A reference to the prior application must be inserted as the first sentence of the specification of this application or in an application data sheet (37 CFR 1.76), if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e) or 120. See 37 CFR 1.78(a). For benefit claims under 35 U.S.C. 120, the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of all nonprovisional applications. Also, the current status of all nonprovisional parent applications referenced should be included.

If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference to the prior application must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This

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time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

### ***Claim Rejections - 35 USC § 102***

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1-6, 9-11, 14-18 and 21-23 are rejected under 35 U.S.C. 102(b) as being anticipated by Stone. Stone teaches a method of preparing substantially non-

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immunogenic soft tissue xenograft compositions. Soft tissue xenografts are defined as meniscus and articular cartilage, ligaments such as the anterior cruciate ligament, tendons and heart valves. Each one is further specifically defined; for example, meniscal cartilage soft tissue in column 1, lines 29-32 as, "The medial and lateral menisci are structures comprised of cells called fibrochondrocytes and an extracellular matrix of collagen and elastic fibers as well as a variety of proteoglycans". This 'theme' that each particular soft tissue suitable for soft tissue xenografts is a collagen containing soft tissue that also possesses a variety of proteoglycans and/or other glycol proteins can be found in the definition of each particular soft tissue described. For example, articular cartilage soft tissue in column 2, lines 14-17; ligament soft tissue in column 3, lines 17-19; and heart valve soft tissue in column 3 lines 50-52. Therefore the method and compositions according to Stone, as will be described below, is directed toward 'collagen-containing material' as claimed in the instant claims of the present application.

The method according to Stone is described as follows, the source of the collagen containing soft tissue xenografts is collected from freshly killed animals (column 10, line 10-12) using sterile technique. The xenograft is washed in cold water, followed by room temperature alcohol (column 10, lines 52-56). After immersion in alcohol, the tissue can be implanted, or alternatively subjected to the following, where if one or more is performed, the order does not matter: radiation treatment, treatment with alcohol or ozonation, cellular disruption via freeze/thaw cycles, and /or treatment with a chemical cross-linking agent such as glutaraldehyde (col. 11, lines 4-10). As an additional method step, the soft tissue xenograft may be treated by gamma radiation in

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an amount of about 0.5-3.0 MegaRad (col. 11, lines 11-15) in order to sterilize the tissue composition. Furthermore, Stone describes an additional method step in the preparation of soft tissue collagen-containing compositions as follows:

“Optionally, the cellular disruption treatment precedes or follows digestion of the xenograft with glycosidases to remove first surface carbohydrate moieties from the xenograft. With respect to the soft tissue xenograft, in addition or in lieu of the glycosidase treatment, the soft tissue xenograft is treated with proteoglycan-depleting factors. Further, the glycosidase and/or proteoglycan-depleting factor digestion (the latter for soft tissue xenografts only) in turn is optionally followed by linkage with capping molecules such as fucosyl or n-acetyl glucosamine molecules to cap surface N-acetylglucosamine end of carbohydrate chains of the xenograft”.

Furthermore, on the specific point of ‘injectable’, the only treatment of the collagen containing material to prepare it for injection is described in paragraph [0060] where the material is treated with proteolytic enzymes. Stone describes the exact same treatment of soft or bone tissue prior to implantation and therefore the treatment of soft tissue (see column 15, lines 51-57), which is a collagen-containing material, is in the exact same state as collagen-containing material of the present invention.

Therefore, as has been described above, the limitations of the rejected claims have been met since Stone describes the composition and methods of making the compositions of collagen-containing soft tissue that is prepared from dead non-human animal tissue and can be used for introduction/injection into humans.

#### ***Claim Rejections - 35 USC § 103***

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. Claims 7-8, 12-13 and 19-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stone and in further view of Odland.

The method and composition of Stone is described in detail as laid out in the rejection above. However, Stone does not teach the use of e-beam ionization radiation in a dose approximately equal to 17.8 kGy for the sterilization of collagen containing soft tissue xenografts.

Odland teaches a method for sterilizing biological tissues using E-beam radiation (electron beam radiation) by using accelerating electron systems such as Van de Graaf generators, Dynamitrons, or linear particle accelerators (see Col. 2, lines 52-55).

A person of ordinary skill in the art at the time the invention was made would have been motivated to use the method of e-beam sterilization in place of gamma radiation sterilization as taught by Stone because Odland teaches that the integrity of collagen containing material is maintained by this sterilization method and because it is much quicker to use this sterilization technique.

Typically the biological tissue is subjected to one-sided exposure to the electron beam, until a sterilizing dose of radiation is absorbed. Odland teaches the use of the approximately 25-28 kGy in his preferred sterilization method as this is in accordance with what the FDA requires for sterilization of medical products (see col. 6, lines 1-9). However, he further points out that effective sterilization doses may be easily

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determined using conventional microbiological techniques, such as including suitable biological indicators in the radiation batch, or can the dose can be determined using radiochromic dye films (see col. 6, lines 29-36). Therefore, would be obvious to adapt the dose to the specific biological tissue, therefore if 17.8 kGy is the optimum dose it would be obvious to use this amount. Furthermore, Odland shows that the integrity of collagen in a biological tissue (porcine aortic leaflets) is maintained after sterilization with 25 kGy of E-beam radiation (see Col. 9, Example 2, and Table 1). Finally, Odland teaches that the use of E-beam radiation for sterilization is much quicker than with gamma radiation because gamma radiation requires a low dose rate in combination with a high exposure periods (see column 3, lines 7-13).

Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use the method of E-beam radiation as taught by Odland and apply it with the methods and teaching of Stone so as to either use E-beam radiation as an alternative or as a supplemental sterilization technique to gamma radiation sterilization of collagen-containing soft tissue.

### **Conclusion**

9. No claim is allowed.
10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suzanne M. Mayer, Ph.D. whose telephone number is 571-272-2924. The examiner can normally be reached Monday to Friday from 8.30am to 5.00pm.

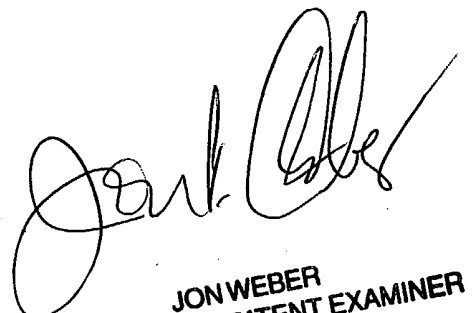


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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

*Smm*  
SMM  
14 September, 2004

  
JON WEBER  
SUPERVISORY PATENT EXAMINER